REMARKS

I. Status of Claims

Claims 1-10 are currently pending. Claims 11 and 12 are canceled without prejudice herein. Claim 7 has been amended herein. That amendment is fully supported in the specification and does not add new matter.

II. Claim Rejections

Rejection under 35 U.S.C. § 112, first paragraph

Claims 7, 8, 11 and 12 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. (Office Action at p. 3.) In particular, the Examiner appears to take issue with the terms "micturition, neurological, musculoskeletal, psychiatric or cognition disorders." (Office Action at p. 6.) Applicants respectfully traverse this rejection.

Without conceding the propriety of the rejection, Applicants have canceled claims 11 and 12 herein. Therefore, the rejection with respect to those claims is rendered moot. Claim 7 has been amended herein to delete "micturition, neurological, musculoskeletal, psychiatric or cognition disorders" from the list of diseases. The remaining diseases are fully supported and enabled in the specification.

For example, the compounds of the present invention are prodrugs of 4-(6-hydroxyindan-1-ylmethyl)-1*H*-imidazole, which has been previously disclosed in U.S. Patent No. 6,313,311 as an α_2 agonist. *See e.g.,* specification at p. 1. U.S. Patent No. 6,313,311 discloses that 4-(6-hydroxyindan-1-ylmethyl)-1*H*-imidazole and other drugs disclosed therein are useful in the treatment of, for example, hypertension, glaucoma,

migraine, diarrhea, ischemia, addiction to chemical substances, and anxiety, and as a sedative or analgesic agent, as a nasal decongestant, and as an adjunct to anesthesia. See col. 1, ll. 15-23 and col. 11, ll. 1-24. 4-(6-hydroxyindan-1-ylmethyl)-1*H*-imidazole finds utility for the treatment of hypotension, shock, and cardiopulmonary resuscitation as disclosed in the specification at p. 1. See also WO 01/30347, already of record. Clonidine, a known α_2 agonist, has been demonstrated useful in the treatment of withdrawal symptoms. Lal, H. et al., *Psychopharmacology of Clonidine*, Alan R. Liss, Inc., New York, NY, 1981, pp. 285-306, a copy of which is submitted herewith. Finally, the activity of the sympathetic nervous system is reduced by α_2 agonists. The usefulness of reduction of the activity of the sympathetic nervous system in treating heart failure is disclosed in Esler M. et al., *J. Auton. Nerv. Syst.,* 72 (1998) 210, a copy of which is also submitted herewith.

Thus, it was known at the time of the present invention that α_2 agonists could be used in the treatment of the diseases and conditions recited in the present claims. The claimed compounds are prodrugs of α_2 agonists. And the specification teaches that compounds of the present invention are metabolized in vivo to form active α_2 agonists. *See id.* at p. 9, Experiment 4. Consequently, the present description enables one of skill in the art to make and use the claimed invention.

For at least these reasons, the rejection should be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 7, 8, 11, and 12 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which the applicant regards as the invention. (Office Action at pp. 8-9.) The Examiner states that the full scope of the disorders which classify "micturition, neurological, musculoskeletal, psychiatric or cognition disorders" is unclear. In addition, the Examiner states that claim 11 fails to specify which disease or condition is being treated. *Id.* Applicants respectfully traverse this rejection.

Without conceding the propriety of the rejection, Applicants have canceled claims 11 and 12 herein. Therefore, the rejection with respect to those claims is rendered moot. In addition, Applicants have amended claim 7 to delete "micturition, neurological, musculoskeletal, psychiatric or cognition disorders". Consequently, this rejection is rendered moot and should be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1, 2, 7, 9, and 11 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over JP 10-195056 to Aono et al. ("Aono"). In support of that rejection, the Examiner states that Aono teaches structurally similar imidazole compounds and "[o]ne skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful in treating, for example, various cancers." (Office Action at p. 11.) Applicants respectfully traverse this rejection.

As mentioned above, claim 11 has been canceled without prejudice herein. Therefore, the rejection of that claim is rendered moot and should be withdrawn.

The Examiner indicates that "[t]he indiscriminate selection of 'some' among 'many' is *prima facie* obvious." (Office Action at p. 11, citations omitted.) However,

Applicants point out that Aono discloses indan compounds substituted with -X-B and -Y-R, wherein X and Y are any divalent radical. That description includes an inordinate number of possible compounds. Aono's broad disclosure of a genus of indan compounds does not render obvious the present claims.

Furthermore, Aono does not teach or suggest to one of skill in the art the claims of the present invention. Indeed, the specific compounds disclosed in Aono **teach away** from the compounds of claims 1 and 2. Not one of the specific compounds disclosed in Aono possesses the substitution pattern of the present compounds. The heterocyclic ring of the Aono compounds is connected via a nitrogen atom, whereas the compounds of the present invention are connected via a carbon atom to the imidazole ring. Similarly, the -OC(O)R group of the present invention and corresponding -Y-R group of Aono does not have the same connectivity to the benzene ring in any of the examples of Aono. Consequently, one of skill in the art would have no reason to choose among the many possible compounds of Aono to arrive at the present invention.

Moreover, Aono fails to disclose all of the claim limitations of the present invention, a requirement necessary to establish a *prima facie* case of obviousness. M.P.E.P. § 2143. In particular, Aono teaches that the compounds disclosed therein may be used for the treatment of various cancers. However, Aono is wholly silent to the treatment of other disease or conditions, including those claimed in the present application (e.g., claims 7 and 9). For this additional reason, Aono does not render obvious the present claims.

For at least these reasons, the rejection should be withdrawn.

III. Conclusions

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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